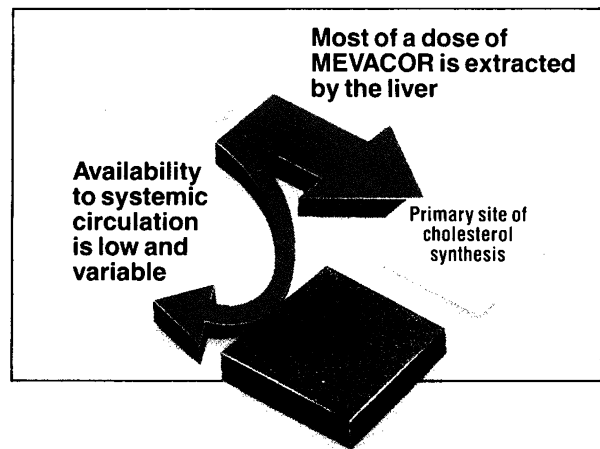


**MEVACOR works where it should:
at the primary site of cholesterol synthesis**

HIGHLY SELECTIVE

MEVACOR is the first agent to selectively inhibit cholesterol production at the primary site of synthesis. This selective activity means MEVACOR is highly effective—with only a low and variable amount of active drug available for systemic circulation.



MEVACOR is contraindicated in patients who are hypersensitive to any component of the medication; in patients with active liver disease or unexplained persistent transaminase elevations; in pregnant or lactating patients; and in women of childbearing age, except when such patients are highly unlikely to conceive.

In clinical studies, marked persistent increases (to more than three times the upper limit of normal) in serum transaminases occurred in 1.9% of adult patients who received lovastatin for at least one year. It is recommended that liver function tests be performed before treatment begins, every 4 to 6 weeks during the first 15 months of therapy, and periodically thereafter in all patients.

For complete details on MEVACOR, including cautionary information regarding myopathy, drug interactions, and slit-lamp monitoring, please refer to the Prescribing Information.

For a Brief Summary of Prescribing Information, please see the back of this advertisement.

For many patients with primary hypercholesterolemia (Types IIa and IIb), when diet and other nondrug therapies are inadequate

MEVACOR[®]
(LOVASTATIN | MSD)

TABLETS, 20 mg 40 mg

MEVACOR® (LOVASTATIN | MSD)



CONTRAINDICATIONS: Hypersensitivity to any component of this medication.

Active liver disease or unexplained persistent elevations of serum transaminases.

Pregnancy and lactation.

Atherosclerosis is a chronic process and the discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Moreover, cholesterol and other products of the cholesterol biosynthesis pathway are essential components for fetal development, including synthesis of steroids and cell membranes. Because of the ability of inhibitors of HMG-CoA reductase such as MEVACOR® (Lovastatin, MSD) to decrease the synthesis of cholesterol and possibly other products of the cholesterol biosynthesis pathway, MEVACOR® should be avoided in women who are pregnant or planning to get pregnant. Therefore, lovastatin is contraindicated during pregnancy. Lovastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive. If the patient becomes pregnant while taking this drug, lovastatin should be discontinued and the patient should be apprised of the potential hazard to the fetus.

WARNINGS: Liver Dysfunction: Marked persistent increases (to more than 3 times the upper limit of normal) in serum transaminases occurred in 1.9% of adult patients who received lovastatin for at least one year in clinical trials (see ADVERSE REACTIONS). When the drug was interrupted or discontinued in these patients, the transaminase levels usually fell slowly to pretreatment levels. The increases usually appeared 3 to 12 months after the start of therapy with lovastatin and were not associated with jaundice or other clinical signs or symptoms. There was no evidence of hypersensitivity. A liver biopsy was done in one of these patients and showed areas of focal hepatitis. In this patient, transaminase levels returned to normal following discontinuation of therapy. Some of these patients had abnormal liver function tests prior to lovastatin therapy and/or consumed substantial quantities of alcohol.

It is recommended that liver function tests be performed before treatment begins, every 1 to 6 weeks during the first 15 months of therapy with lovastatin, and periodically thereafter in all patients. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients, measurements should be repeated promptly and then performed more frequently. If the transaminase levels show evidence of progression, particularly if they rise to 3 times the upper limit of normal and are persistent, the drug should be discontinued. Liver biopsy should be considered if elevations are persistent beyond the discontinuation of the drug.

The drug should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease. Active liver disease or unexplained transaminase elevations are contraindications to the use of lovastatin.

As with other lipid-lowering agents, moderate (less than 3 times the upper limit of normal) elevations of serum transaminases have been reported following therapy with MEVACOR (see ADVERSE REACTIONS). These changes appeared soon after initiation of therapy with MEVACOR, were often transient, were not accompanied by any symptoms, and interruption of treatment was not required.

Skeletal Muscle: Several cases of rhabdomyolysis have been associated with lovastatin therapy alone, when combined with immunosuppressive therapy including cyclosporine in cardiac transplant patients, and when combined in non-transplant patients with either gemfibrozil or lipid-lowering doses (≥ 1 g/day) of niacin. Acute renal failure from rhabdomyolysis has been seen more commonly with the lovastatin-gemfibrozil combination and has also been reported in transplant patients receiving lovastatin plus cyclosporine.

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with lovastatin. Therefore, patients receiving concomitant lovastatin and erythromycin should be carefully monitored.

Fulminant rhabdomyolysis has been seen as early as 3 weeks after initiation of combined therapy with gemfibrozil and lovastatin but may be seen after several months. For these reasons, it is felt that, in most subjects who have had an unsatisfactory lipid response to either drug alone, the possible benefits of combined therapy with lovastatin and gemfibrozil do not outweigh the risks of severe myopathy, rhabdomyolysis, and acute renal failure. While it is not known whether this interaction occurs with fibrates other than gemfibrozil, myopathy and rhabdomyolysis have occasionally been associated with the use of other fibrates alone, including clofibrate. Therefore, the combined use of lovastatin with other fibrates should generally be avoided.

Physicians contemplating combined therapy with lovastatin and lipid-lowering doses of niacin should be advised that severe myopathy should carefully weigh the potential benefits and risks and should carefully monitor patients for any signs and symptoms of muscle pain, tenderness, or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration of either drug. Periodic CPK determinations may be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy. The monitoring of lovastatin drug and metabolite levels may be considered in transplant patients who are treated with immunosuppressives and lovastatin.

Lovastatin therapy should be temporarily withheld or discontinued in any patient with an acute, serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis, including severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine, and electrolyte disorders, and uncontrolled seizures.

Myalgia has been associated with lovastatin therapy. Transient, mildly elevated creatine phosphokinase levels are commonly seen in lovastatin-treated patients. However, in clinical trials, approximately 0.5% of patients developed a myopathy, i.e., myalgia or muscle weakness associated with markedly elevated CPK levels. Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness, or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. Lovastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.

Most of the patients who have developed myopathy (including rhabdomyolysis) while taking lovastatin were receiving concomitant therapy with immunosuppressive drugs, gemfibrozil, or lipid-lowering doses of niacin. In clinical trials, about 30% of patients on concomitant immunosuppressive therapy including cyclosporine developed myopathy; the corresponding percentages for gemfibrozil and niacin were approximately 5% and 2%, respectively.

In 6 patients with cardiac transplants taking immunosuppressive therapy including cyclosporine concomitantly with lovastatin 20 mg/day, the average plasma level of active metabolites derived from lovastatin was elevated to approximately 4 times the expected levels. Because of an apparent relationship between increased plasma levels of active metabolites derived from lovastatin and myopathy, the daily dosage in patients taking immunosuppressants should not exceed 20 mg/day (see DOSAGE AND ADMINISTRATION). Even at this dosage, the benefits and risks of using lovastatin in patients taking immunosuppressants should be carefully considered.

PRECAUTIONS: General: Before instituting therapy with MEVACOR® (Lovastatin, MSD), an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, weight reduction in obese patients, and to treat other underlying medical problems (see INDICATIONS AND USAGE).

Lovastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with lovastatin.

Eye: There was a high prevalence of baseline lenticular opacities in the patient population included in the clinical trials with lovastatin. During these trials the appearance of new opacities was noted. The causal relationship of lovastatin to these findings has not been established.

Of 431 patients examined with slit lamp at baseline and during therapy with lovastatin, 34 had opacities reported at the final examination (5 to 15 months after starting lovastatin) that were not noted at baseline. On the other hand, in 45 patients, opacities observed at baseline were not noted at the final examination, so that the prevalence did not increase. There was no clinically significant change in visual acuity in the patients who had new opacities reported, nor was any patient, including those with opacities noted at baseline, discontinued from therapy because of a decrease in visual acuity. Nevertheless, until further experience is obtained, it is recommended that patients placed on lovastatin therapy be examined with a slit lamp before or shortly after initiation of treatment and annually thereafter.

Homozygous Familial Hypercholesterolemia: MEVACOR is less effective in patients with the rare homozygous familial hypercholesterolemia, possibly because these patients have no functional LDL receptors. MEVACOR appears to be more likely to raise serum transaminases (see ADVERSE REACTIONS) in these homozygous patients.

Drug Interactions: Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin. See WARNINGS, Skeletal Muscle.

Coumarin Anticoagulants: In a clinical trial in warfarin-treated patients designed specifically to observe a potential effect of lovastatin on the prothrombin time, lovastatin in doses up to 40 mg b.i.d. did not produce any consistent alteration of the anticoagulant action of warfarin. However, since the drug was marketed, clinically evident bleeding and/or increased prothrombin time have been reported in a few patients taking coumarin anticoagulants concomitantly with lovastatin. The causal relationship to lovastatin is unclear. Nevertheless, it is recommended that in patients taking anticoagulants, prothrombin time be determined before starting lovastatin and frequently enough during early therapy to insure that no significant alteration of prothrombin time occurs. Once a stable prothrombin time has been documented, prothrombin times can be monitored at the intervals usually recommended for patients on coumarin anticoagulants. If the dose of lovastatin is changed, the same procedure should be repeated. Lovastatin therapy has not been associated with bleeding or with changes in prothrombin time in patients not taking anticoagulants.

Antipyrine: Antipyrine is a model for drugs metabolized by the microsomal hepatic enzyme system (cytochrome P450 system). Because lovastatin had no effect on the pharmacokinetics of antipyrine, interactions with other drugs metabolized via this mechanism are not expected.

Propranolol: In normal volunteers, there was no clinically significant pharmacokinetic or pharmacodynamic interaction with concomitant administration of single doses of lovastatin and propranolol.

Digoxin: In patients with hypercholesterolemia, concomitant administration of lovastatin and digoxin resulted in no effect on digoxin plasma concentrations.

Other Concomitant Therapy: Although specific interaction studies were not performed, in clinical studies, lovastatin was used concomitantly with beta blockers, calcium channel blockers, diuretics, and nonsteroidal anti-inflammatory drugs (NSAIDs) without evidence of clinically significant adverse interactions.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 21-month carcinogenicity study in mice, a statistically significant ($p < 0.05$) increase in the incidence of hepatocellular carcinomas and adenomas was observed at doses of 500 mg/kg/day (312 times the maximum recommended human dose) of lovastatin. These changes were not seen in mice given doses of 20 and 100 mg/kg/day (12.5 and 62.5 times the maximum recommended human dose).

A statistically significant increase ($p < 0.05$) in the incidence of pulmonary adenomas was seen in female mice receiving 500 mg/kg/day (312 times the maximum recommended human dose); no similar changes were seen in males at any dose or in females receiving 20 or 100 mg/kg/day (12.5 or 62.5 times the maximum recommended human dose). Because the incidence of pulmonary tumors was within the range of untreated animals in studies of similar duration, the relationship of this latter change to treatment is not known.

In addition, an increase in the incidence of papilloma in the non-glandular mucosa of the stomach was observed in mice receiving 100 and 500 mg/kg/day (62.5 and 312 times the maximum recommended human dose); no increase was seen at a dosage of 20 mg/kg/day (12.5 times the maximum recommended human dose). The glandular mucosa was not affected. The human stomach contains only glandular mucosa. Importantly, there is a strong association between this change and hyperplasia of the squamous epithelium (acanthosis) in this region; acanthosis is a characteristic change observed in the non-glandular mucosa of rodents treated with HMG-CoA reductase inhibitors and is most probably a result of inhibition of the reductase in this tissue.

Similar squamous epithelium is found in the esophagus and anorectal junction of the mouse and rat; however, no evidence of a similar drug-induced hyperplastic response was observed in these tissues in studies of up to 21 months in the mouse given up to 500 mg/kg/day (312 times the maximum recommended human dose), or in a study of 24 months in the rat given 180 mg/kg/day (112 times the maximum recommended human dose).

In a 24-month carcinogenicity study in rats, there was a positive dose response relationship for hepatocellular carcinogenicity in males (unadjusted $p = 0.025$). However, because the incidence of hepatocellular carcinogenicity observed in male rats in this study is similar to that observed spontaneously in this strain of rat, the implications of this finding are unclear.

No evidence of mutagenicity was observed in a microbial mutagen test using mutant strains of *Salmonella typhimurium* with or without rat or mouse liver metabolic activation. In addition, no evidence of damage to genetic material was noted in an *in vitro* alkaline elution assay using rat or mouse hepatocytes, a V-79 mammalian cell forward mutation study, an *in vitro* chromosome aberration study in CHO cells, or an *in vivo* chromosome aberration assay in mouse bone marrow.

No drug-related effects on fertility were found in studies with rats.

Pregnancy: Pregnancy Category X: See CONTRAINDICATIONS.

Lovastatin has been shown to produce skeletal malformations in the rat fetus at doses of 800 mg/kg/day (500 times the maximum recommended human dose). At similar doses in mice, an increase in skeletal malformations was observed. These individual changes are within the range of those observed spontaneously in this strain of mouse. No drug-induced changes were seen in either species at doses of up to 80 mg/kg/day (50 times the maximum recommended human dose). No evidence of malformations was noted in rabbits at up to 15 mg/kg/day (highest tolerated dose—about 9 times the maximum recommended human dose). There are no data in pregnant women.

Nursing Mothers: Studies in rats have shown that lovastatin is excreted in the milk. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from MEVACOR, women taking lovastatin should not nurse their infants (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in children have not been established. Because children are not likely to benefit from cholesterol lowering for at least a decade and because experience with this drug is limited (no

studies in subjects below the age of 20 years), treatment of children with lovastatin is not recommended at this time.

ADVERSE REACTIONS: MEVACOR® (Lovastatin, MSD) is generally well tolerated; adverse reactions usually have been mild and transient. Less than 1% of patients were discontinued from controlled clinical studies due to adverse experiences attributable to MEVACOR. About 2% of patients were discontinued from all studies (controlled and uncontrolled) due to adverse experiences attributable to MEVACOR; about one-third of these patients were discontinued due to increases in serum transaminases.

Clinical Adverse Experiences: Adverse experiences reported in patients treated with MEVACOR in controlled clinical studies are shown in the table below.

	MEVACOR (N = 613) %	Placebo (N = 82) %	Cholestyramine (N = 88) %	Probucol (N = 97) %
Gastrointestinal				
Constipation	4.9	—	34.1	2.1
Diarrhea	5.5	4.9	8.0	10.3
Dyspepsia	3.9	—	13.6	3.1
Flatulence	6.4	2.4	21.6	2.1
Abdominal pain/cramps	5.7	2.4	5.7	5.2
Heartburn	1.6	—	8.0	—
Nausea	4.7	3.7	9.1	6.2
Musculoskeletal				
Muscle cramps	1.1	—	1.1	—
Myalgia	2.4	1.2	—	—
Nervous System/Psychiatric				
Dizziness	2.0	1.2	—	1.0
Headache	9.3	4.9	4.5	8.2
Skin				
Rash/pruritus	5.2	—	4.5	—
Special Senses				
Blurred vision	1.5	—	1.1	3.1
Dysgeusia	0.8	—	1.1	—

Laboratory Tests: Marked persistent increases of serum transaminases have been noted (see WARNINGS).

About 11% of patients had elevations of creatine phosphokinase (CPK) levels of at least twice the normal value on one or more occasions. The corresponding values for the control agents were cholestyramine, 9% and probucol, 2%. This was attributable to the noncardiac fraction of CPK. Large increases in CPK have sometimes been reported (see WARNINGS, Skeletal Muscle).

Concomitant Therapy: In controlled clinical studies in which lovastatin was administered concomitantly with cholestyramine, no adverse reactions were reported to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with lovastatin or cholestyramine. Other lipid-lowering agents were not administered concomitantly with lovastatin during controlled clinical studies. In uncontrolled clinical studies, most of the patients who have developed myopathy were receiving concomitant therapy with immunosuppressive drugs, gemfibrozil, or niacin (nicotinic acid) (see WARNINGS, Skeletal Muscle).

Uncontrolled Clinical Studies: The adverse experiences observed in uncontrolled studies were similar to those seen in controlled clinical studies. Abnormal liver function tests were observed at a higher incidence than in the controlled studies (see WARNINGS, Liver Dysfunction). Myopathy (myalgia with marked CPK elevations) was reported in approximately 0.5% of patients (see WARNINGS, Skeletal Muscle).

Causal Relationship Unclear: **Nervous System:** Peripheral neuropathy has been reported; the relationship to lovastatin is uncertain. Visual evoked response, nerve conduction measurements, and electromyography in over 30 patients showed no evidence of neurotoxic effects of lovastatin.

Special Senses: Of 431 patients examined with slit lamp at baseline and during therapy with lovastatin, 34 had opacities reported at the final examination (5 to 15 months after starting lovastatin) that were not noted at baseline. On the other hand, in 45 patients, opacities observed at baseline were not noted at the final examination, so that the prevalence did not increase (see PRECAUTIONS).

Post-marketing Experience: Additional adverse experiences occurring since the drug was marketed are listed below:

Clinical Adverse Experiences

Gastrointestinal: Hepatitis, cholestatic jaundice, anorexia, vomiting.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus-like syndrome, polymyalgia rheumatica, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, flushing, malaise, and dyspnea.

Nervous System/Psychiatric: Psychic disturbances, including anxiety, paresthesia.

Skin: Erythema multiforme, including Stevens-Johnson syndrome, toxic epidermal necrolysis.

Causal Relationship Unknown

Gastrointestinal: Pancreatitis, stomatitis.

Skin: Alopecia.

Nervous System/Psychiatric: Depression, insomnia.

Metabolic: Edema.

Clinical Laboratory Test Findings

Liver Function Tests: Liver function test abnormalities, including elevated alkaline phosphatase and bilirubin.

Thyroid Function Tests: Rare reports of thyroid function test abnormalities in patients taking concomitant thyroxine.

OVERDOSAGE: The oral LD₅₀ of MEVACOR in mice is 20 g/kg.

Five healthy human volunteers have received up to 200 mg of lovastatin as a single dose without clinically significant adverse experiences. A few cases of accidental overdosage have been reported; no patients had any specific symptoms, and all patients recovered without sequelae. The maximum dose taken was 5 to 6 g.

Until further experience is obtained, no specific treatment of overdosage with MEVACOR can be recommended.

The dialyzability of lovastatin and its metabolites in man is not known at present.

DOSAGE AND ADMINISTRATION: The patient should be placed on a standard cholesterol-lowering diet before receiving MEVACOR and should continue on this diet during treatment with MEVACOR. MEVACOR should be given with meals.

The recommended starting dose is 20 mg once a day given with the evening meal. The recommended dosing range is 20 to 80 mg/day in single or divided doses; the maximum recommended dose is 80 mg/day. Adjustments of dosage should be made at intervals of 4 weeks or more. Doses should be individualized according to the patient's response (see Tables I to IV under CLINICAL PHARMACOLOGY, Clinical Studies for dose response results).

For those patients with severely elevated serum cholesterol levels (i.e., > 300 mg/dL [7.8 mmol/L] on diet), MEVACOR may be initiated at 40 mg/day.

In patients taking immunosuppressive drugs concomitantly with lovastatin (see WARNINGS, Skeletal Muscle), the maximum recommended dosage is 20 mg/day.

Cholesterol levels should be monitored periodically and consideration should be given to reducing the dosage of MEVACOR if cholesterol levels fall below the targeted range.

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For more detailed information, consult your MSD Representative or see Prescribing Information, Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19386. JOMC48R(510)

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Action: Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon® is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

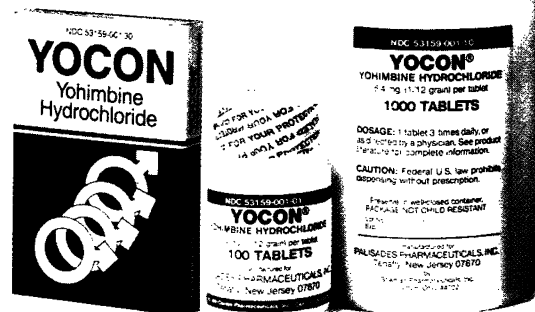
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of YOCON® 1/12 gr. 5.4mg in bottles of 100's NDC 53159-001-01, 1000's NDC 53159-001-10 and Blister-Paks of 30's NDC 53159-001-30

References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological Basis of Therapeutics 6th ed., p. 176-188, McMillan December Rev. 1/85.
3. Weekly Urological Clinical Letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

Rev. 1/85



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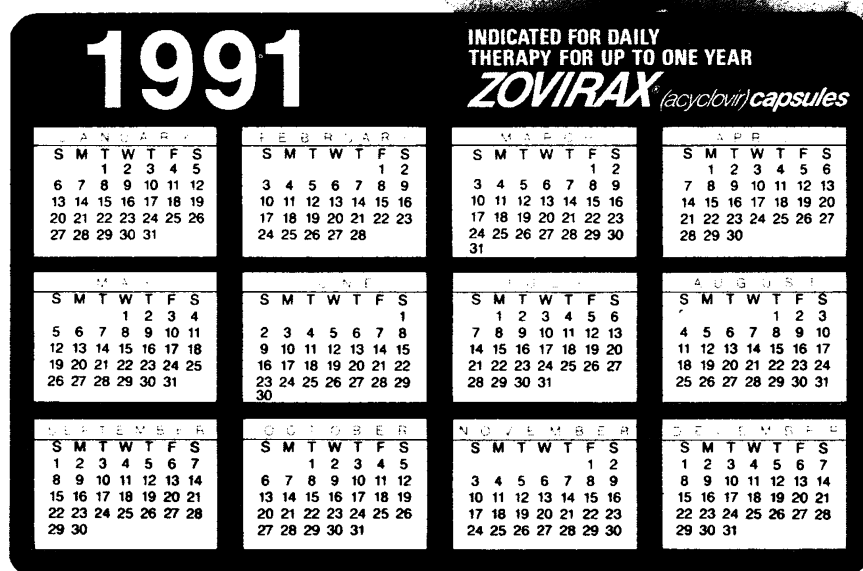
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*Please see brief summary of prescribing information on adjacent page. Clinical success rate for bronchitis and pneumonia was 98%. Data on file. Medical Department, SmithKline Beecham Pharmaceuticals.
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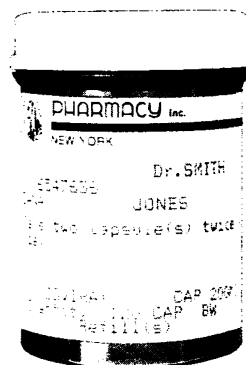
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*Alternate maintenance regimens range from 200 mg t.i.d. to 200 mg five times daily.

¹In a controlled study of 3 years' duration, 45%, 52%, and 63% of patients remained free of recurrences in the first, second, and third years, respectively.³

Please see brief summary of prescribing information on adjacent page.



ZOVIRAX[®]
(acyclovir) capsules

KEEPS HERPES PATIENTS LESION-FREE LONGER[†]

ZOVIRAX® CAPSULES

ZOVIRAX® SUSPENSION

(ACYCLOVIR)

BRIEF SUMMARY

INDICATIONS AND USAGE: Zovirax Capsules and Suspension are indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.

Zovirax Capsules and Suspension are also indicated for the acute treatment of herpes zoster (shingles).

Genital Herpes Infections: The severity of disease is variable depending upon the immune status of the patient, the frequency and duration of episodes, and the degree of cutaneous or systemic involvement. These factors should determine patient management, which may include symptomatic support and counseling only, or the institution of specific therapy. The physical, emotional and psycho-social difficulties posed by herpes infections as well as the degree of debilitation, particularly in immunocompromised patients, are unique for each patient, and the physician should determine therapeutic alternatives based on his or her understanding of the individual patient's needs. Thus orally administered Zovirax is not appropriate in treating all genital herpes infections. The following guidelines may be useful in weighing the benefit/risk considerations in specific disease categories:

First Episodes (primary and nonprimary infections—commonly known as initial genital herpes):

Double-blind, placebo-controlled studies have demonstrated that orally administered Zovirax significantly reduced the duration of acute infection (detection of virus in lesions by tissue culture) and lesion healing. The duration of pain and new lesion formation was decreased in some patient groups. The promptness of initiation of therapy and/or the patient's prior exposure to Herpes simplex virus may influence the degree of benefit from therapy. Patients with mild disease may derive less benefit than those with more severe episodes. In patients with extremely severe episodes, in which prostration, central nervous system involvement, urinary retention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with intravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in patients with frequent recurrences (6 or more episodes per year) have shown that orally administered Zovirax given daily for 4 months to 3 years prevented or reduced the frequency and/or severity of recurrences in greater than 95% of patients.

In a study of 283 patients who received 400 mg (two 200 mg capsules) twice daily for 3 years, 45%, 52% and 63% of patients remained free of recurrences in the first, second and third years, respectively. Serial analyses of the 3 month recurrence rates for the 283 patients showed that 71% to 87% were recurrence-free in each quarter, indicating that the effects are consistent over time.

The frequency and severity of episodes of untreated genital herpes may change over time. After 1 year of therapy, the frequency and severity of the patient's genital herpes infection should be re-evaluated to assess the need for continuation of acyclovir therapy. Re-evaluation will usually require a trial off acyclovir to assess the need for re-institution of suppressive therapy. Some patients, such as those with very frequent or severe episodes before treatment, may warrant uninterrupted suppression for more than a year.

Chronic suppressive therapy is most appropriate when, in the judgment of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, orally administered Zovirax should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the relevance to humans of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given high parenteral doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients with annual re-evaluation.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

Herpes Zoster Infections: In a double-blind, placebo-controlled study of 187 normal patients with localized cutaneous zoster infection (93 randomized to Zovirax and 94 to placebo), Zovirax (800 mg 5 times daily for 10 days) shortened the times to lesion scabbing, healing and complete cessation of pain, and reduced the duration of viral shedding and the duration of new lesion formation.

In a similar double-blind, placebo-controlled study in 83 normal patients with herpes zoster (40 randomized to Zovirax and 43 to placebo), Zovirax (800 mg 5 times daily for 7 days) shortened the times to complete lesion scabbing, healing, and cessation of pain, reduced the duration of new lesion formation, and reduced the prevalence of localized zoster-associated neurologic symptoms (paresthesia, dyesthesia or hyperesthesia).

CONTRAINDICATIONS: Zovirax Capsules and Suspension are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulations.

WARNINGS: Zovirax Capsules and Suspension are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high parenteral doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS—Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex and varicella-zoster isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex or varicella-zoster virus to acyclovir and clinical response to therapy has yet to be established (see CLINICAL PHARMACOLOGY-Microbiology).

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced. The clinical effects of this combination have not been studied.

Carcinogenesis, Mutagenesis, Impairment of Fertility: The data presented below include references to peak steady state plasma acyclovir concentrations observed in humans treated with 800 mg given orally 6 times a day (dosing appropriate for treatment of herpes zoster) or 200 mg given orally 6 times a day (dosing appropriate for treatment of genital herpes). Plasma drug concentrations in animal studies are expressed as multiples of human exposure to acyclovir at the higher and lower dosing schedules (see Pharmacokinetics).

Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of up to 450 mg/kg administered by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. At 450 mg/kg/day, plasma concentrations were 3 to 6 times human levels in the mouse bioassay and 1 to 2 times human levels in the rat bioassay.

Acyclovir was tested in two *in vitro* cell transformation assays. Positive results were observed at the highest concentration tested (31 to 63 times human levels) in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative (40 to 80 times human levels) in the other, possibly less sensitive, transformation assay.

In acute cytogenetic studies, there was an increase, though not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of acyclovir (100 mg/kg) in rats (62 to 125 times human levels) but not in Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters (380 to 760 times human levels). In addition, no activity was found after 5 days dosing in a dominant lethal study in mice (36 to 73 times human levels). In all 4 microbial assays, no evidence of mutagenicity was observed. Positive results were obtained in 2 of 7 genetic toxicity assays using mammalian cells *in vitro*. In human lymphocytes, a positive response for chromosomal damage was seen at concentrations 150 to 300 times the acyclovir plasma levels achieved in man. At one locus in mouse lymphoma cells, mutagenicity was observed at concentrations 250 to 500 times human plasma levels. Results in the other five mammalian cell loci follow: at 3 loci in a Chinese hamster ovary cell line, the results were inconclusive at concentrations at least 1850 times human levels; at 2 other loci in mouse lymphoma cells, no evidence of mutagenicity was observed at concentrations at least 1500 times human levels.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). In the mouse study plasma levels were 9 to 18 times human levels, while in the rat study they were 8 to 15 times human levels. At a higher dose in the rat (50 mg/kg/day, s.c.), there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day (16 to 31 times human levels). No effect upon implantation efficiency was observed when the same dose was administered intravenously (53 to 106 times human levels). In a rat peri- and postnatal study at 50 mg/kg/day s.c. (11 to 22 times human levels), there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F₁ generation. Although not statistically significant, there was also a dose-related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size (plasma levels were not measured). However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits (53 to 106 times human levels), no drug-related reproductive effects were observed.

Intraperitoneal doses of 80 or 320 mg/kg/day acyclovir given to rats for 6 and 1 months, respectively, caused testicular atrophy. Plasma levels were not measured in the one month study and were 24 to 48 times human levels in the six month study. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. At 100 mg/kg/day plasma levels were 47 to 94 times human levels, while at 200 mg/kg/day they were 159 to 317 times human levels. No testicular abnormalities were seen in dogs given 50 mg/kg/day i.v. for one month (21 to 41 times human levels) and in dogs given 60 mg/kg/day orally for one year (6 to 12 times human levels).

Pregnancy: Teratogenic Effects: Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rabbit (50 mg/kg/day, s.c. and i.v.) or in standard tests in the rat (50 mg/kg/day, s.c.). These exposures resulted in plasma levels 9 and 18, 16 and 106, and 11 and 22 times, respectively, human levels. In a non-standard test in rats, there were fetal abnormalities, such as head and tail anomalies, and maternal toxicity. In this test, rats were given 3 s.c. doses of 100 mg/kg acyclovir on gestation day 10, resulting in plasma levels 63 and 125 times human levels. There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in standard animal studies, the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: Acyclovir concentrations have been documented in breast milk in two women following oral administration of Zovirax and ranged from 0.6 to 4.1 times corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg/day. Caution should be exercised when Zovirax is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Herpes Simplex: Short-Term Administration: The most frequent adverse reactions reported during clinical trials of treatment of genital herpes with orally administered Zovirax were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%).

Nausea and/or vomiting occurred in 2 of 287 (0.7%) patients who received placebo.

Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments with orally administered Zovirax (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in a clinical trial for the prevention of recurrences with continuous administration of 400 mg (two 200 mg capsules) 2 times daily for 1 year in 586 Zovirax-treated patients were: nausea (4.8%), diarrhea (2.4%), headache (1.9%) and rash (1.7%). The 589 control patients receiving intermittent treatment of recurrences with Zovirax for 1 year reported diarrhea (2.7%), nausea (2.4%), headache (2.2%) and rash (1.5%). The most frequent adverse reactions reported during the second year by 390 patients who elected to continue daily administration of 400 mg (two 200 mg capsules) 2 times daily for 2 years were headache (1.5%), rash (1.3%) and paresthesia (0.8%). Reactions reported by 329 patients during the third year include asthenia (1.2%), paresthesia (1.2%) and headache (0.9%).

Herpes Zoster: The most frequent adverse reactions reported during three clinical trials of treatment of herpes zoster (shingles) with 800 mg of oral Zovirax 5 times daily for 7 to 10 days in 323 patients were: malaise (11.5%), nausea (8.0%), headache (5.9%), vomiting (2.5%), diarrhea (1.5%) and constipation (0.9%). The 323 placebo recipients reported malaise (11.1%), nausea (11.5%), headache (11.1%), vomiting (2.5%), diarrhea (0.3%) and constipation (2.4%).

OVERDOSAGE: Precipitation of acyclovir in renal tubules may occur when the solubility (2.5 mg/mL) in the intratubular fluid is exceeded. Renal lesions considered to be related to obstruction of renal tubules by precipitated drug crystals occurred in the following species: rats treated with i.v. and i.p. doses of 20 mg/kg/day for 21 and 31 days, respectively, and at s.c. doses of 100 mg/kg/day for 10 days; rabbits at s.c. and i.v. doses of 50 mg/kg/day for 13 days; and dogs at i.v. doses of 100 mg/kg/day for 31 days. A 6 hr hemodialysis results in a 60% decrease in plasma acyclovir concentration. Data concerning peritoneal dialysis are incomplete but indicate that this method may be significantly less efficient in removing acyclovir from the blood. In the event of acute renal failure and anuria, the patient may benefit from hemodialysis until renal function is restored (see DOSAGE AND ADMINISTRATION).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: 200 mg (one 200 mg capsule or one teaspoonful [5 mL] suspension) every 4 hours, 5 times daily for 10 days.

Chronic suppressive therapy for recurrent disease: 400 mg (two 200 mg capsules or two teaspoonfuls [10 mL] suspension) 2 times daily for up to 12 months, followed by re-evaluation. See INDICATIONS AND USAGE and PRECAUTIONS for considerations on continuation of suppressive therapy beyond 12 months. Alternative regimens have included doses ranging from 200 mg 3 times daily to 200 mg 5 times daily.

Intermittent Therapy: 200 mg (one 200 mg capsule or one teaspoonful [5 mL] suspension) every 4 hours, 5 times daily for 5 days. Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Acute Treatment of Herpes Zoster: 800 mg (four 200 mg capsules or four teaspoonfuls [20 mL] suspension) every 4 hours orally 5 times daily for 7 to 10 days.

Patients With Acute or Chronic Renal Impairment: Comprehensive pharmacokinetic studies have been completed following intravenous acyclovir infusions in patients with renal impairment. Based on these studies, dosage adjustments are recommended in the following chart for genital herpes and herpes zoster indications:

Normal Dosage Regimen (5x daily)	Creatinine Clearance (mL/min/1.73m ²)	Adjusted Dosage Regimen	
		Dose (mg)	Dosing Interval (hrs)
200 mg every 4 hours	> 10	200	every 4 hours, 5x daily
	0-10	200	every 12 hours
800 mg every 4 hours	> 25	800	every 4 hours, 5x daily
	10-25	800	every 8 hours
	0-10	800	every 12 hours

For patients who require hemodialysis, the dosing schedule should be adjusted so that a dose is administered after each dialysis.

References: 1. Mertz GJ, Jones CC, Mills J, et al. Long-term acyclovir suppression of frequently recurring genital herpes simplex virus infection: a multicenter double-blind trial. *JAMA*. 1988;260:201-206. 2. Mertz GJ, Eron L, Kaufman R, et al. Prolonged continuous versus intermittent oral acyclovir treatment in normal adults with frequently recurring genital herpes simplex virus infection. *Am J Med*. 1988;85(suppl 2A):14-19. 3. Data on file, Burroughs Wellcome Co., 1990.

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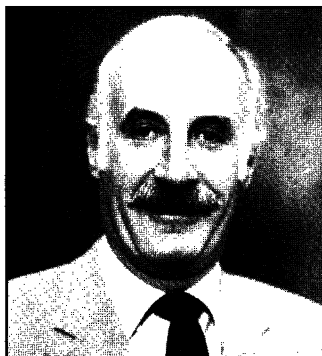
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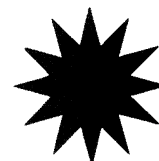
Sun Valley, Idaho—July 25-27, 1991



DAVID M. BARTON, MD
President
Idaho Medical Association

An Invitation to Sun Valley

We are pleased to extend to you a cordial invitation to attend the 99th Annual Meeting of the Idaho Medical Association in the beautiful setting of Idaho's Sun Valley. An excellent scientific session has been planned that should appeal to all types of physicians—primary care physicians and specialists alike. It should be a good opportunity not only to enjoy beautiful Sun Valley, but also receive six credit hours of Category I at an informative scientific session.



S C H E D U L E

THURSDAY, JULY 25, 1991

8:30 AM - 5:00 PM HOUSE OF DELEGATES

SCIENTIFIC SESSION - FRIDAY, JULY 26, 1991

- 7:45 AM WELCOME—David M. Barton, MD
- 8:00 AM RHEUMATOID ARTHRITIS
James Louie, MD
Chief, Division of Rheumatology,
UCLA School of Medicine
- 8:50 AM GASTROESOPHAGEAL REFLUX DISORDERS
Michael Levitt, MD
Associate Chief of Staff for Research
VAMC Minneapolis, Professor of Medicine,
University of Minnesota
- 9:40 AM RECESS TO REVIEW EXHIBITS
- 10:10 AM CA RISK FACTORS IN ESTROGEN REPLACEMENT
R. Donald Gambrell, Jr., MD
Clinical Professor, Department of Endocrinology,
Medical College of Georgia
- 11:00 AM PHYSICIAN CONCERNS: ETHICS OF AIDS
Roy Schwarz, MD
Senior Vice President, Medical Education and Science,
American Medical Association
- 11:50 AM MORNING WRAP-UP
- 12:00 NOON LUNCH BREAK
- 1:30 PM GAS AND BLOATING
Michael Levitt, MD
- 2:20 PM RENOIR: HIS ART AND HIS ARTHRITIS
James Louie, MD
- 3:00 PM OSTEOARTHRITIS AND ESTROGEN
R. Donald Gambrell, Jr., MD

SATURDAY, JULY 27, 1991

8:30 AM CLOSING SESSION, HOUSE OF DELEGATES

Registration Fee: \$150.00 for non-IMA members and out-of-state physicians
For Information Contact: Idaho Medical Association, P.O. Box 2668, Boise, ID 83701
Telephone: (208) 344-7888

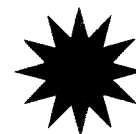
FACULTY

James Louie, MD
Chief
Division of Rheumatology
UCLA School of Medicine

Michael Levitt, MD
Associate Chief of
Staff for Research
VAMC Minneapolis
Professor of Medicine
University of Minnesota

R. Donald Gambrell, Jr., MD
Clinical Professor
Department of Endocrinology
Medical College of Georgia

Roy Schwarz, MD
Senior Vice President
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Idaho Medical Association July 25-27, 1991 Sun Valley Reservation Request

Confirmed reservations require an advance deposit equal to one night's room rental. Please send deposit, along with this entire form to: **SUN VALLEY RESERVATIONS OFFICE, SUN VALLEY, IDAHO 83353**. A confirmation of room reservations will be forwarded on receipt of deposit. **PLEASE MAKE RESERVATIONS EARLY FOR BEST SELECTION!** If accommodations requested are not available, the next comparable accommodations will be substituted.

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Three-bdrm (up to 6)	\$270/day

Sun Valley Condominiums

Studio (up to 2)	\$ 95/day
One-bdrm (up to 2)	\$125 day
Two-bdrm (up to 4)	\$142 day
Three-bdrm (up to 6)	\$184 day
Four-bdrm (up to 8)	\$220/day

*(Condos: Atelier, Cottonwood, Dollar Meadows,
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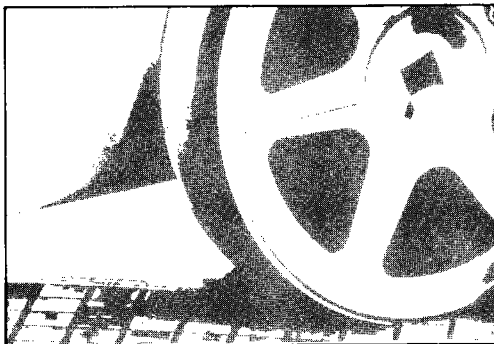
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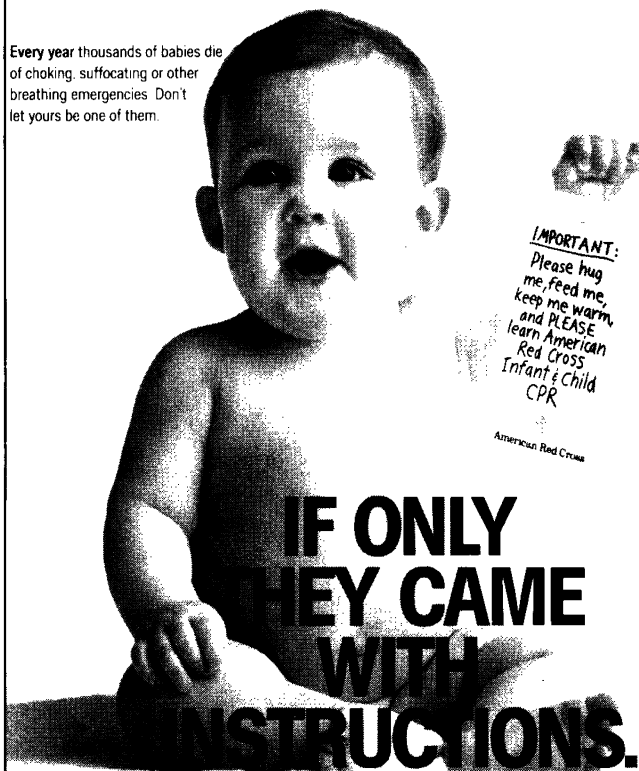
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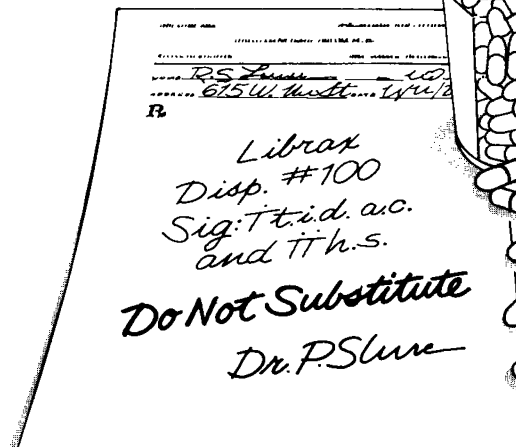
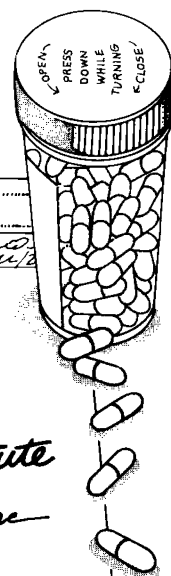


American Red Cross



Specify Adjunctive

LIBRAX[®]



Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium bromide.

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.
Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.
Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving).

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.

As with all anticholinergics, inhibition of lactation may occur.

Withdrawal symptoms of the barbiturate type have occurred after discontinuation of benzodiazepines (see Drug Abuse and Dependence).

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary.

Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established. Inform patients to consult physician before increasing dose or abruptly discontinuing this drug.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated; avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

Drug Abuse and Dependence: Withdrawal symptoms similar to those noted with barbiturates and alcohol have occurred following abrupt discontinuance of chlordiazepoxide; more severe seen after excessive doses over extended periods; milder after taking continuously at therapeutic levels for several months. After extended therapy, avoid abrupt discontinuation and taper dosage. Carefully supervise addiction-prone individuals because of predisposition to habituation and dependence.

Revised: February 1968

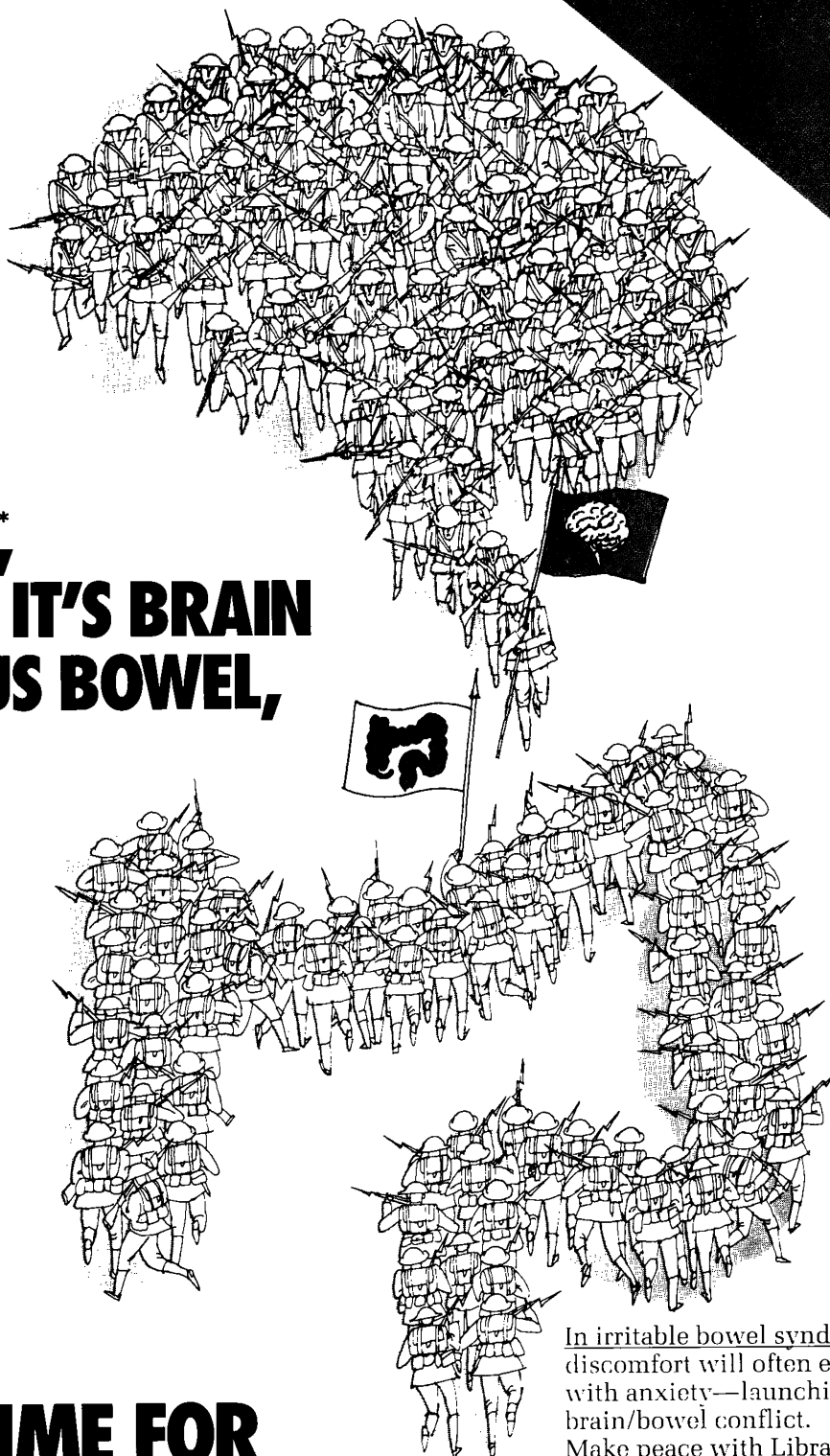


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*Librax has been evaluated as possibly effective as adjunctive therapy in the treatment of peptic ulcer and IBS.

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Each capsule contains 5 mg chlordiazepoxide
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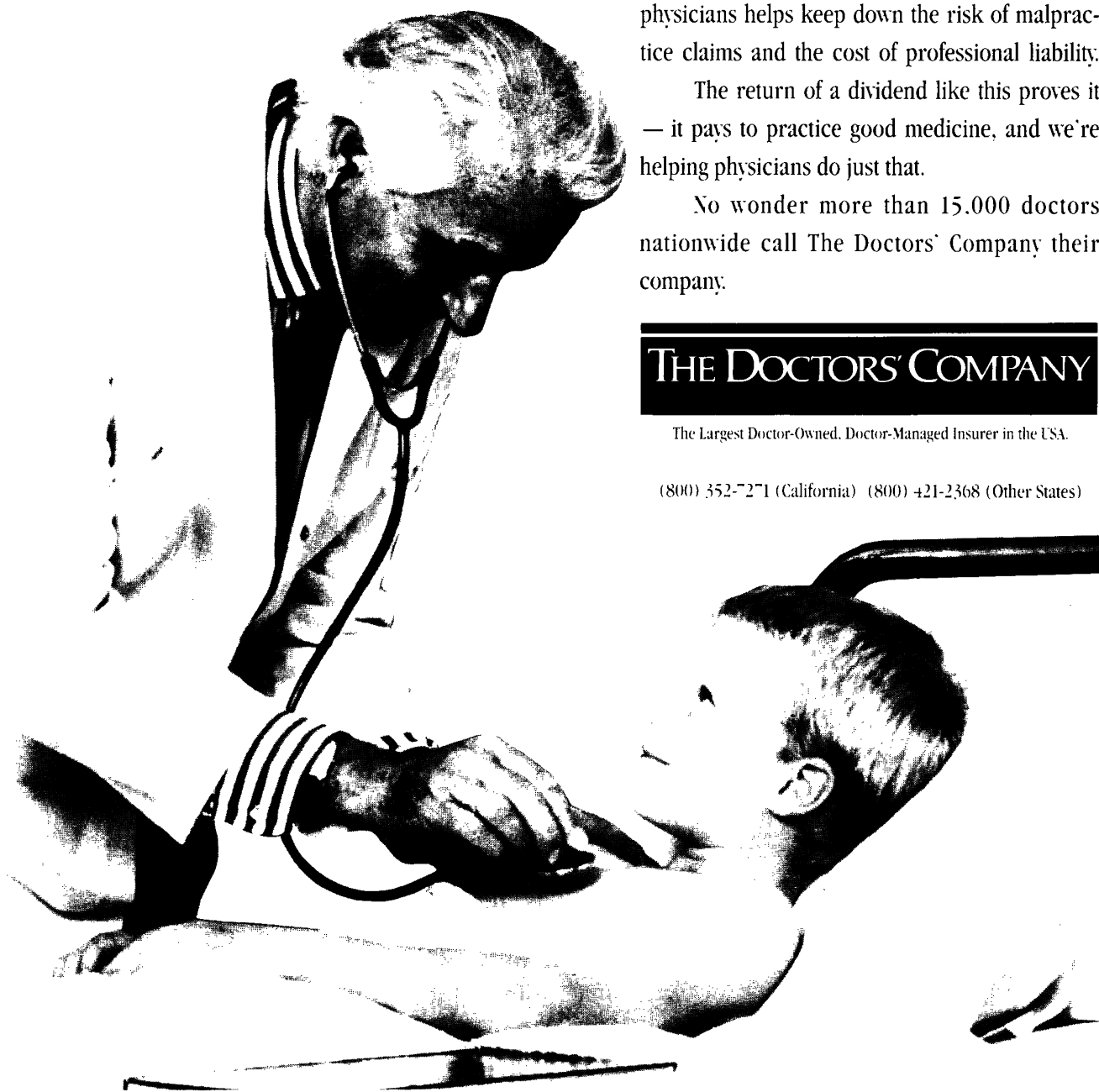


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Please see summary of prescribing information on adjacent page.

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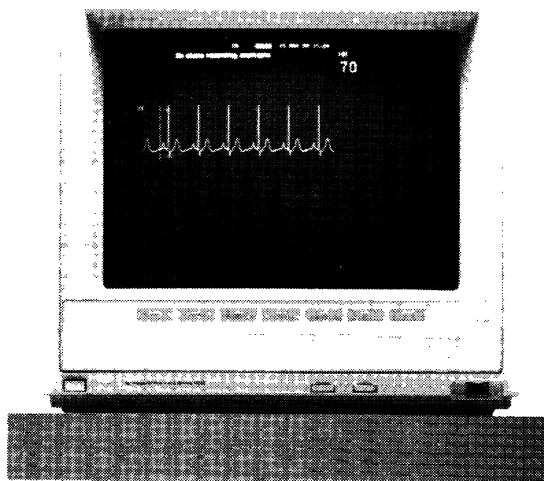
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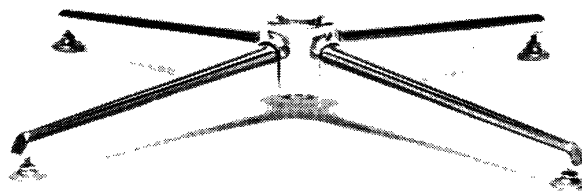
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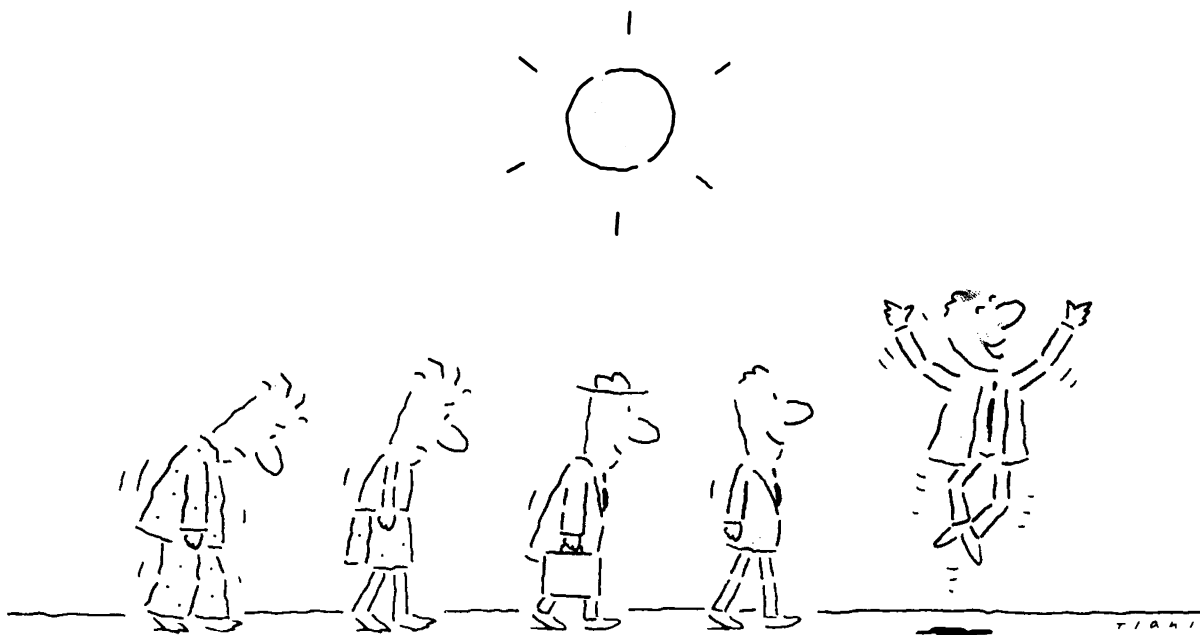
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PEDIATRICIANS—Southern California. Challenging career opportunities for Pediatricians desiring private practice. Growing, prestigious, university-affiliated south bay medical center is recruiting BC/BE physicians for expanding solo and group practices. Excellent compensation. Submit CV to J. Michaels, 2600 Cliff Dr, Newport Beach, CA 92663.

HEALTH OFFICER—\$5514-\$6701 per month. Requires a California physician license and experience/training equivalent to five years responsible experience as practicing physician or two years with a public health agency. Within 60 days of hire, must obtain California certification to supervise physician's assistants. Apply immediately to Yuba County Personnel, 215 5th St, Marysville, CA 95901; (916) 741-6281. EOE.

TWO INTERNISTS seek an associate BE/BC Internist for busy Internal Medicine group practice located in a community of 60,000. Forty miles from San Francisco. Excellent modern hospital. Superb location in which to live and work. For more information write Thomas I. Paukert, MD, 3443 Villa Lane, Ste 6, Napa, CA 94558; (707) 252-8407.

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SACRAMENTO, CALIFORNIA MEDICAL/LEGAL DISABILITY EVALUATIONS. Opportunities available in Sacramento for BC physicians in Dermatology, Internal Medicine, Orthopedics, Ophthalmology, Otolaryngology, Psychiatry, Toxicology, and Neurology with a multispecialty medical group which provides forensic medical evaluations. This is an excellent opportunity to supplement income as well as associate with a well respected medical group whose practice is limited to evaluations. Send inquiry and CV to Terence Doyle, Disability Reporters, 2805 J St, Ste 305, Sacramento, CA 95816; (916) 444-8600.

NORTHERN CALIFORNIA

San Jose's leading multispecialty group is growing. We are seeking BE/BC physicians in the following specialties:

- Urgent Care
- Family Practice
- Internal Medicine
- Ob/Gyn

If you are committed to excellence and strongly motivated for success, we would like to hear from you. Please send your CV to Maureen Forrester, San Jose Medical Group, Inc, 45 S 17th St, San Jose, CA 95112; or call (408) 282-7833.

UNIVERSITY OF CALIFORNIA, DAVIS MEDICAL CENTER. The University of California, Davis, Department of Emergency Medicine is searching for physicians residency trained or BC in Emergency Medicine. The Health Science Campus is located in Sacramento and serves a large area of northern California. The Emergency Department cares for over 60,000 patients a year. The Center operates as a Level One Trauma Center, has paramedic base station training responsibilities, and has a helicopter service. An approved Emergency Medicine Residency Program began in July 1990. Emergency Physicians supervise medical students, interns, and residents, in addition to having direct patient responsibilities. Support for clinical research is available to those interested. University compensation is competitive, and fringe benefits include health and dental insurance, three weeks paid vacation, one week continuing medical education, social security, UC retirement plan, 12 paid holidays per year, and full malpractice coverage. Send CV to Robert W. Derlet, MD, Chief, Division of Emergency Medicine, University of California, Davis, Medical Center, 2315 Stockton Blvd, Sacramento, CA 95817.

CALIFORNIA, MONTEREY BAY. Full-/part-time positions available with Monterey Bay's largest and most successful Urgent Care network. Generous guarantee, incentive plan, and benefit package. Malpractice covered. Practice in California's most beautiful coastal recreational area. BC/BE Emergency Room Medicine or Family Practice specialists preferred. Contact Bob Morris, MD, FACEP, Doctors on Duty Medical Clinics, 223 Mt Hermon Rd, Scotts Valley, CA 95066; (408) 438-9341.



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The continuing growth of our service area population (now 90,000) has created an immediate need for additional BC/BE physicians in the following specialties:

- FAMILY PRACTICE
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- OTOLARYNGOLOGY
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- NEUROLOGY

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OREGON. General Internal Medicine and Family Practice, BC/BE, sought for 10 member, multispecialty group in beautiful rural community, population 16,500, 38 miles southwest of Portland. Send CV to Administrator, 420 E. Fifth St, McMinnville, OR 97128; (503) 472-6161.

ARIZONA OPPORTUNITIES TO EQUAL YOUR AMBITIONS. Thomas-Davis Medical Centers, PC, a rapidly expanding multispecialty group practice of 150 plus physicians in 14 clinic locations throughout Arizona has positions available in Family Practice, Internal Medicine, Otolaryngology, OB/GYN, and Orthopedics. Exceptional fringe benefits, profit sharing, and retirement program. Guarantee for first two years, plus incentive. Early shareholder. Fee-for-service, as well as physician owned HMO. Must be BC/BE. Call or write Bill De Long at Thomas-Davis Medical Centers, PC, PO Box 12650, Tucson, AZ 85732; 1 (800) 658-9166.

FAMILY PRACTICE, BC/BE to join group practice in growing southwestern town. Full service clinic, 280-bed hospital. Offering competitive salary, equal call schedule, partnership. Contact Myrna Hughes, Arizona Western Medical Center, 2149 W. 24th St, Yuma, AZ 85364; (602) 344-1400.

BEAUTIFUL MONTEREY BAY. Immediate opportunity for a friendly, skilled, Family Practice or Emergency Physician to join highly respected Urgent Care group with two beautiful Santa Cruz clinics. Committed to high quality care. Nice people, flexible scheduling, comprehensive benefits, including paid malpractice, group health insurance, long-term disability insurance, no nights, rapid advancement to full partnership in an outstanding place to live. Please send CV to Stuart Simon, MD, 6800 Soquel Dr, Aptos, CA 95003; or call (408) 662-3611.

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PHYSICIANS WANTED

CALIFORNIA

Primary Care Physicians and Radiologists needed to work as *locum tenens* statewide. High salary, paid malpractice. Work whenever and wherever you wish. Permanent placements as well. **Western Physicians Registry: Northern California**, contact Jim Ellis, Director, (415) 601-7676 or (800) 437-7676. **Southern California**, contact Tracy Zweig, Director, (805) 643-9346 or (800) 635-3175.

EMERGENCY MEDICINE PHYSICIAN. Seeking full-time Emergency Medicine Physician with a minimum of five years experience working full-time in high volume (40,000 annual visits or more), high-acuity Emergency Department, with at least two years of surgical training. Physician must be willing to accept rural assignments and make a five year commitment. Physician must have excellent references for medical competence, references required. Must be willing to work nights. Salary \$50.00 to \$75.00 per hour. Qualified applicants send résumé to Nancy Rickards, Director of Physician Services, Arizona Emergency Physicians, Ltd, 2222 S Dobson Rd, Ste 1100, Mesa, Arizona 85202. (Job location: Arizona) Proof of authorization to practice in US required if hired.

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ORTHOPAEDIST—BC/BE for expanding San Francisco bay area practice emphasizing Occupational Medicine and medical-legal evaluation seeks full-time nonsurgery practicing Orthopaedist. Outstanding reputation, facilities and support staff, established referral base. Unique income opportunities. Submit CV and letter stating professional goals and availability to: Administrator, 2040 Polk St, Box 337, San Francisco, CA 94109.

FAMILY PHYSICIANS WANTED. We have opportunities for placement in California. We specialize only in Family Practice placement. Send CV to Family Physician Placement Services, 1528 Brookhollow Dr, Ste 58, Santa Ana, CA 92705; or call 1 (800) 422-1143.

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SAN FRANCISCO BAY AREA. Energetic, recently trained BC/BE General Internist needed for 12 MD satellite of Palo Alto Medical Clinic, a 150 physician multispecialty group with a national reputation for innovation and excellence. Broad inpatient/outpatient Internal Medicine practice in growing Bay Area community. Excellent location with convenient access to San Francisco and Stanford. Competitive compensation/benefits package. Early partnership. Please send CV to David Hooper, PAMC Fremont Center, 39500 Liberty St, Fremont, CA 94538.

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CONTACT: Colleen Mooney, Recruitment Coordinator

Rockwood Clinic, PS

E. 400 Fifth Ave
Spokane, WA 99202
(509) 838-2531

EMERGENCY MEDICINE. Emergency Medicine group seeking career oriented ACLS, ATLS certified physician for an immediate opening. Moderate volume; income \$140,000 plus. Great outdoor activities including hunting, fishing, boating, skiing, sailing, camping, and hiking in south central Washington on the Columbia River. Send CV to Kennewick Emergency Physicians, PS, PO Box 6192, Kennewick, WA 99336-6192; or call (509) 627-1798.

SAN JOAQUIN VALLEY. Excellent opportunity for Family Practitioner to serve the underserved. No night call or weekends. Competitive salary plus benefits, paid malpractice. Agricultural community, one hour from the mountains, two hours from the coast. Bilingual English-Spanish helpful. Send CV to Hugh F. Stallworth, MD, Fresno County Department of Health, PO Box 11867, Fresno, CA 93775; (209) 445-3202.

NEUROLOGIST—BC/BE, full- or part-time, for expanding San Francisco bay area. Private practice with emphasis on clinical Occupational Neurology and medical-legal evaluations. Expertise in EMG, EEG and EP desired. Excellent reputation, referral base, facilities and support staff. Unique income opportunity. Submit CV and letter stating professional goals, and availability to Personnel, 2040 Polk St, Box 337, San Francisco, CA 94109.

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NEPHROLOGIST WANTS PARTNER/ASSOCIATE BC/BE Gastroenterologist/Cardiologist/Nephrologist/Pulmonologist. Excellent practice, equal partnership opportunity without buy-in or overhead. Send CV to Dr M. Streger, 27800 Medical Center Rd, Ste 122, Mission Viejo, CA 92691.

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OTOLARYNGOLOGIST. BC/BE to join 28 physician multispecialty group practice. Located in beautiful Pacific northwest between Seattle and Vancouver, BC. Contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

(Continued on Page 753)

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PHYSICIANS WANTED

OB/GYN. BC/BE to join 20 physician (OB, Pediatrics, Internal Medicine) practice in sunny central Washington. Reasonable call schedule with three OB/GYN department. Loan repayment program available. Competitive salary, excellent benefit package including vacation at 30 days per year and professional liability. Contact Ann Garza, Yakima Valley Farm Workers Clinic, PO Box 190, Toppenish, WA 98948; (509) 865-5898.

OPPORTUNITY for full- and part-time Emergency Physicians. Excellent fee-per-patient load ratio. Malpractice paid. Also, Emergency Department/Family Practice positions for urgent care/industrial center. Send CV to Front Line Community Physicians, PO Box 10610, Santa Ana, CA 92711, or contact Medical Director at (714) 771-3290.

MONTEREY BAY. Immediate opportunity for full-time/part-time Internist/Family Practitioner to join busy, well established and respected group practice. Excellent laboratory and x-ray facilities. Send CV to Thorngate Medical Group, attn. Jean Reynolds, 1011 Cass St, Ste 201, Monterey, CA 93940.

HAWAII. Family Practitioner and Pediatrician needed for rural underserved area. Full-time position in non-profit community health clinic. No OB, hospitalizations optional. Desire dedicated person to work in multicultural setting. Contact Alan Chun, MD, Waianae Coast Comprehensive Health Center, 86-260 Farington Hwy, Waianae, HI 96792; (808) 696-7081.

OB/GYN, INTERNISTS, Family Practitioners, Pediatricians for Arizona and western opportunities. Quality positions available other regions of country. Inquiries confidential. Mitchell & Associates, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080.

RADIOLOGIST. Part-time position available immediately in small hospital with general Radiography and Fluoroscopy, Mammography, and Ultrasound in Weaverville, California. Contact Drs Wheeler, Biggs, or Babbitt, West Coast Radiology, 3798 Janes Rd, Ste 12, Arcata, CA 95521; office number (707) 822-3621, ext 191.

MULTIPLE FAMILY PRACTICE (BC/BE) positions available in several suburban satellite clinics of a large Seattle area multispecialty group practice. Diverse patient population includes managed care, fee-for-service, and retired military (at some satellite clinics). Competitive salary and excellent benefits. Contact Mary Anderson, Pacific Medical Center, 1200 12th Ave S., Seattle, WA 98144; (206) 326-4111.

URGENT CARE/PRIMARY CARE PHYSICIANS for over 90 positions available with various physician groups in Phoenix metropolitan/Tucson, Arizona. Excellent compensation and partnership opportunities. Contact Mitch Young, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080.

OB/GYN. Multispecialty group in northwest Washington desires second Obstetrician. Excellent practice opportunity, full range of benefits, early partnership status, all practice costs paid. For more information contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

BC/BE FAMILY PRACTITIONER, OB-competent, for nonprofit community clinic in California redwood country. Rural but sophisticated university town. Contact Donald Verwayen, Northcountry Clinic, 785 18th St, Arcata, CA 95521; (707) 822-2481.

MEDICAL DIRECTOR TRAUMA SERVICES. Eden Hospital. Level II Regional Trauma Center, Alameda county. Submit CV to Trauma Services, Eden Hospital, 20103 Lake Chabot Rd, Castro Valley, CA 94546; or call Dr Peter Wong, (415) 886-0535 or Dr Brian Walker, (415) 881-8445.

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Fred Whitmore, CEO
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or send CV to:
West Park Hospital
707 Sheridan Ave
Cody, WY 82414.
EOE.

NEWPORT BEACH. Start up opportunity to associate with a busy General Internist. Flexible terms. Please send CV to John Homan, MD, 351 Hospital Rd, #411, Newport Beach, CA 92663; (714) 548-1278.

CLINIC PHYSICIAN—SOLANO COUNTY, CALIFORNIA. (Salary \$4911 to \$5969 per month.) Solano County Health Services Department currently has an opening for Clinic Physician-MCH Director and full- and part-time Clinic Physicians. Please contact Solano County Human Resources Department, 580 Texas St, Fairfield, CA 94533; (707) 421-6170. EOE/AA

HOUSE PHYSICIAN. Seton Medical Center is a fully accredited 350-bed facility that serves a diverse patient population from San Francisco and the peninsula. Position available immediately for third physician to share 24-hour house coverage. Hours negotiable. Current California license and general medicine background required. BE in Family Practice or Internal Medicine highly desired. Malpractice insurance paid. Competitive salary. Sponsored and operated by the Daughters of Charity of St Vincent de Paul. Equal opportunity employer. Send CV to Kathy Green, Manager, Employment, Seton Medical Center, 1900 Sullivan Ave, Daly City, CA 94015.

NORTHERN CALIFORNIA GENERAL SURGEON. Opportunity for General Surgeon with thoracic and vascular experience. Salary leading to partnership. Surgical group in northern California rural community. Excellent quality of life. Reply to 1165 S Dora, Ste A-3, Ukiah, CA 95482; (707) 462-7579.

GALLUP-THOREAU-GRANTS, NEW MEXICO: SCENIC CORRIDOR TO NORTHWESTERN NEW MEXICO. National forests, Indian culture and historic sites await Family Practitioner/General Practitioner in a community health center system. Contact New Mexico Health Resources, Box 27650, Albuquerque, NM 87125; (505) 260-0993. Not-for-profit, no fee placement assistance.

FACULTY POSITIONS. Well established, fully accredited, 18 resident program seeking full-time faculty. Program is affiliated with UC Davis and located in Stockton, California. Candidate must be BC/BE. Teaching and OB experience preferred, but not required. Responsibilities include resident teaching, patient care, administration, and research development. Send CV to Bruce S. Nickols, MD, Family Practice Department, San Joaquin General Hospital, PO Box 1020, Stockton, CA 95201; (209) 468-6834. AA/EOE.

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Irwin P. Goldstein, MD, Associate Medical Director, SCPMG, KAISER PERMANENTE, Department 057, Walnut Center, Pasadena, CA 91188-8013; or call 1 (800) 541-7946.

PHYSICIANS WANTED

INTERNAL MEDICINE. A prime Internal Medicine practice awaits you in sunny, metropolitan Phoenix, Arizona. We have additional Internal Medicine opportunities in picturesque Wisconsin and Ohio. Competitive income guarantee. Available benefits include malpractice insurance, CME allowance, relocation expenses assistance, administrative/financial support and more. For confidential inquiry, call 1 (800) 969-7715. Dan Jones, Gielow/Laske Associates, 306 N. Milwaukee St, Milwaukee, WI 53202.

CALIFORNIA. Physician recruiting services available to solo practitioners, single and multispecialty clinics, and hospitals. Placement positions available in some specialties. For information call Bradshaw Associates, 21 Altamont, Orinda, CA 94563; (415) 376-0762.

OPPORTUNITY FOR ENERGETIC, ENTREPRENEURIAL PRACTITIONER to establish new practice at the El Dorado Medical Village (a 20,000 square foot office complex) located between the hospitals in Stockton. Historic, rapidly growing community of 300,000 located on the Delta waterways between the San Francisco bay and the Sierra Nevada mountains. Call Bill Campbell; (209) 462-6130, or (415) 574-0320.

BOULDER COLORADO—BC/BE FAMILY PRACTICE PHYSICIAN for busy clinic serving low income and underserved people. Position includes faculty appointment at the University of Colorado Department of Family Medicine and the opportunity to train residents. Clinic is eight miles from Boulder and 30 miles from Denver, Colorado. Send résumé to CCFHS, 1345 Plaza Ct N, Lafayette, CO 80026; or call Pete Leibig at (303) 665-9310 for more details.

CARDIOLOGY. Invasive Cardiologist join noninvasive; new Cath lab; north bay area. Huge opportunity. Electrophysiologist even better. Résumé to Number 234, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602. ASAP.

PATHOLOGIST, BC/BE—CENTRAL CALIFORNIA VALLEY. Seven member group seeks associate for independent multiple hospital and private laboratory practice. Send CV to Robert F. Chard, MD, Delta Pathology Associates Medical Group, 2291 W. March Ln, Ste 179E, Stockton, CA 95207.

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GENERAL SURGEON position available with large Seattle area multispecialty group practice. Diverse patient population includes managed care, fee-for-service, active duty, and retired military. Competitive salary and excellent benefits. Send CV to Mary Anderson, Pacific Medical Center, 1200 12th Ave S, Seattle, WA 98144; (206) 326-4100.

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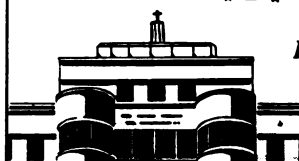
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(Continued from Page 754)

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PRACTICE OPPORTUNITIES. Family Practice, Internal Medicine, and Obstetrics and Gynecology positions available in San Diego, California, Phoenix, Arizona, Seattle, Washington, and Salt Lake City, Utah. Contact Eric Bennett, PO Box 5316, Scottsdale, AZ 85261; (602) 998-4540.

FAMILY PRACTICE RESIDENCY FACULTY POSITION—CASPER, WYOMING. University of Wyoming Family Practice Residency-Casper is seeking an experienced, clinically oriented, BC Pediatrician to be the Pediatric Coordinator of an 8-8 Family Practice residency program. Level II Nursery skills are a must. 60% teaching, 20% direct patient care, 20% research. This is a tenure track position. University approval will be required prior to filling this position. Come join us in beautiful Wyoming. The University of Wyoming is an affirmative action/EOE. Contact Dr David Driggers, Director, University of Wyoming Family Practice Residency, 1522 E. "A" St, Casper, WY 82601; (307) 266-3076.

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MONTEREY BAY AREA—CALIFORNIA MEDICAL/LEGAL DISABILITY EVALUATIONS. Opportunities available in Salinas for BC physicians in Dermatology, Internal Medicine, Orthopedics, Ophthalmology, Otolaryngology, Psychiatry, Toxicology, and Neurology with a multispecialty medical group which provides forensic medical evaluations. This is an excellent opportunity to supplement income as well as associate with a well respected medical group whose practice is limited to evaluations. Send inquiry and CV to Kevin Gerszewski, Disability Reporters, 212 San Jose St, Ste 311, Salinas, CA 93901; (408) 754-0411.

KETCHIKAN, ALASKA. University of Washington-affiliated Family Practice seeking BC Family Physician interested in teaching and providing excellent medical care. Accredited hospital in scenic southeast Alaska. 12 years of Family Medicine students and residents through WAMI program. Fee-for-service practice. Comprehensive benefits. Negotiable salary. Stable community with wide range of activities and opportunities. Contact David Johnson, MD, or Bill Henrickson, MD, Ketchikan Medical Clinic, Inc, 3612 Tongass Ave, Ketchikan, AK 99901; phone collect (907) 225-5145.

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(Continued on Page 757)

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COASTAL CALIFORNIA. San Luis Obispo, Internal Medicine BC/BE, busy multispecialty group, eight miles to beach, excellent schools, recently rated "best small town in USA." Rewarding hospital-based practice. Guaranteed salary, malpractice covered, excellent call rotation. Call or send CV to Fran Wolke, San Luis Obispo General Hospital, PO Box 8113, San Luis Obispo, CA 93403-8113; (805) 549-4936.

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(Continued on Page 758)

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FAMILY PRACTITIONER. IMMEDIATE OPENING outpatient clinic in Asian community. Full-Time, \$64K plus physician's assistant and competitive benefits. Send letter/résumé to Medical Director, Asian Health Services, 310 8th St, Ste 200, Oakland, CA 94607.

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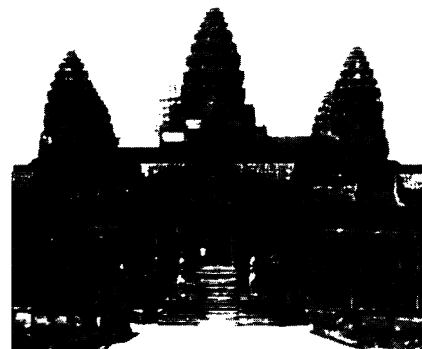
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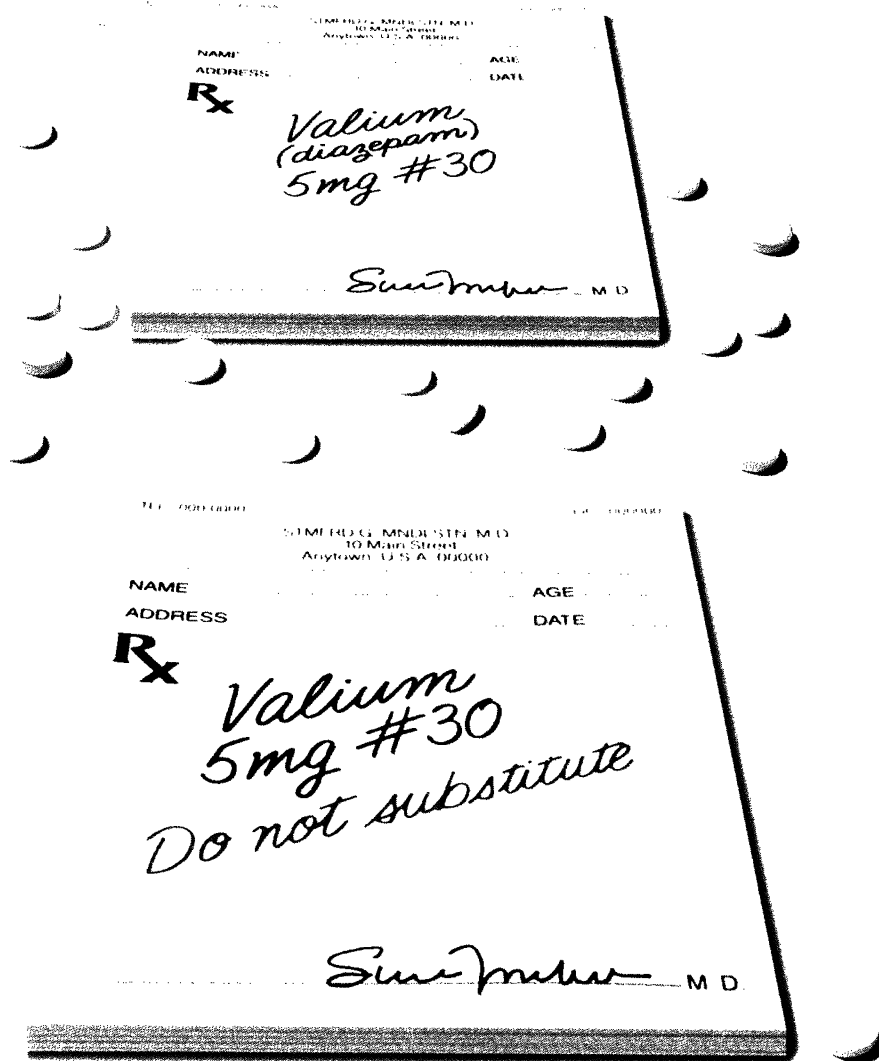
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